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Central Corneal Thickness (CCT) among Glaucoma and Non Glaucoma Patients in a Hospital Based Population

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Abstract:
Objectives: To estimate the difference in the central corneal thickness among normal tension glaucoma (NTG), primary open angle glaucoma (POAG), ocular hypertensives (OHT) and non glaucomatous patients.
Methods: Intraocular pressure (IOP) (by Goldmann applanation tonometry) and central corneal thickness (CCT) (ultrasound Pachymetry, Ocuscan rxp) were measured in 44 eyes with NTG, 138 eyes with POAG, 16 eyes with OHT and in 202 normal eyes. The CCT was used to obtain a corrected value for the IOP. The data thus obtained was analyzed and statistical calculations were performed using statistical software (SPSS version 16).
Results: Total number of study subjects were 400; among those, 202 were normal subjects, 138 were POAG patients, 44 were NTG patients and 16 were ocular hypertensives. Mean CCT in POAG was 543.37µm with SD 37.39µm, and mean CCT in NTG was 530.43µm with SD 33.43, and mean CCT in ocular hypertensives was 598.06µm with SD 5.92 and normal subjects was 539.78µm with SD 23.95. There was higher CCT in ocular hypertensive patients than other groups which was significant (p value <0.001). There was no significant difference in CCT between normal subjects (539.78 µm) and patients with POAG (543.37 µm), but the CCT in the group with NTG (530.43 µm) was lower than that in the normal subjects or the group with POAG but statistically it was not significant (p value >0.001).
Conclusions: patients with OHT have a thicker CCT than do patients with POAG, NTG and normal subjects. The central corneal thickness of the normal tension glaucoma patients was lower than as compared to that in the primary open angle glaucoma patients and normal subjects. No significant difference was found between the primary open angle patients and the normal subjects. Due to the effect of the CCT on the measurement of the IOP with the use of an applanation tonometer, which is the main parameter in the diagnosis and the follow up of glaucoma patients, many POAG patients may be misdiagnosed as NTG due to thinner corneas and the normal patients may be misdiagnosed as OHT due to thicker corneas. Measurement of the central corneal thickness helps the ophthalmologist in making a correct diagnosis for these patients, as well as in better management of the intra ocular pressure, especially when their corneal thicknesses differ markedly from the normal thickness. The inclusion of a CCT adjusted IOP during the management of glaucoma patients, will prevent the over or under treatment of such patients.

Keywords: *Central corneal thickness, Primary open angle glaucoma, Normal tension glaucoma, Ocular Hypertension*

1. Introduction

Glaucoma is one of the major causes of irreversible blindness over the world. According to World Health Organization glaucoma accounts for 13.5% of global blindness over the world. Worldwide, it has become the second most common cause of bilateral blindness. Glaucoma is the third leading cause of blindness in India. 12 million people are affected accounting for 12.8% of the total blindness. Population based studies report a prevalence between 2 to 13 %. Early detection is the only key to preserve the vision.
Even though elevated intraocular pressure (IOP) is no longer included in the current definition, it is still mentioned as an important contributing factor. It is the only risk factor that can be manipulated therapeutically. Intraocular pressure is measured clinically by applanation tonometry.

The thickness of central cornea ranges from 500 microns to 570 microns with standard deviation of 0.04. CCT is a highly heritable trait and varies in different ethnic groups [2, 6]. CCT influences the measurement of IOP in many types of tonometry including Goldman applanation tonometry (GAT) [3, 7]. Goldmann applanation tonometry is accurate for a constant CCT value. So the intraocular pressure will be underestimated in persons with thin cornea because thinner cornea requires less force than expected to achieve applanation [5, 6, 9]. Similarly, intraocular pressure (IOP) will be overestimated in persons with thick cornea because thicker cornea requires more force than expected to achieve applanation [4]. This can lead to the incorrect diagnosis of ocular hypertension in normal patients with thick cornea and normal tension glaucoma in primary open angle glaucoma patients with thin cornea. Hence central corneal thickness measurement is important in the diagnosis and management of glaucoma.

2. Materials and Methods

This descriptive, hospital based study was conducted in Dr. SMCSI Medical College, Karakonam, Trivandrum. Glaucoma patients attending the Eye OPD between November 2013 to October 2015 were included in the study.

2.1. Inclusion Criteria

All patients >40 years newly diagnosed to have Primary open angle glaucoma, Normal tension glaucoma, Ocular hypertensives and the patients attending the Eye OPD for other complaints (not satisfying the exclusion criteria)

2.2. Exclusion Criteria

Those not willing to give informed consent, previous intraocular or corneal surgery, diabetes mellitus, high astigmatism(>2D), secondary glaucoma patients, any other retinal, optic nerve or intracranial disease affecting visual function of the patients. Patients who were already on anti glaucoma medications were also excluded.

Informed consent was obtained from the patients prior to participation in the study.

2.3. Sample Size

The sample size arrived at was 100. It was calculated using the following formula

$$n = (Z2\ 1 - \alpha/2\ (2\ sp\ 2\ )) \times 1/\ d2$$

$$Sp = (s1\ 2 + s2\ 2\ ) \times 1/2$$

S1 = standard deviation of the normal subjects
S2 = standard deviation of the glaucoma groups
Sp = Pooled SD
d = precision required
α = significance level.

A detailed history was taken. A detailed ophthalmic evaluation was done. Visual acuity was assessed monocularly using Snellen's chart. This was followed by a complete ocular examination including pupillary reaction by torch light and anterior segment slit lamp evaluation to rule out causes for secondary glaucoma. Central corneal thickness (CCT) was measured using ultrasonic pachymeter (OcuScanRxP). Intra ocular pressure was measured using Goldmann Applanation Tonometry (GAT) between 8 am and 12 noon. Corrected IOP was calculated using the inbuilt correction factor in the pachymeter. Gonioscopy was done using Goldmann 3 mirror gonioscope. Refraction under cycloplegia was performed in all patients. Cycloplegia was accomplished with one drop Tropicamide-phenylephrine combination and instilled every five minutes for a total of three drops. Retinoscopy was performed after 30 minutes. The posterior segment evaluation in every patient was carried out in a fully dilated state of the eye with direct ophthalmoscopy and 90 D/ 78 D lenses. Visual field chart was obtained by perimetry [Humphrey field analyser] on consecutive visit.

3. Method of Analysing Data

Mean CCT of each category of subjects and standard deviation was estimated. 95% Confidence interval for the estimates was obtained. Difference between the mean thicknesses of CCT was estimated among the four groups. Mean CCT of Non Glaucomatous patients were compared to NTG subjects, Ocular Hypertensives, and to POAG patients. The data was stored on a computerised database and analysed using SPSS Computer software (version16.0). One-way ANOVA was used in the statistical analysis and a p value of below 0.05 was considered as significant.

4. Results and Observations

In this study, we recruited 200 participants with and without Glaucoma. Among these recruited participants, 91 glaucoma patients, 8 ocular Hypertensives, and 101 normals.

Participants were further classified according to gender as, 93 (46.5%) male and 107 (53.5%) female (Table 8) (Figure 15).

Gender	Frequency	Percent
Male	93	46.5
Female	107	53.5

Table 1: Participants Classified According To Gender

Participants	Frequency (%)
Glaucoma/OHT present	198 (49.5%)
Normal	202 (50.5%)

Table 2: Participants Classified According to Clinical Diagnosis (400 Eyes)

Diagnosis	Frequency (%)
POAG	138 (34.5)
NTG	44 (11.0)
OHT	16 (4.0)

Table 3: Classification of Glaucoma Eyes and Ocular Hypertensives According to IOP Measurement and Fundus Findings

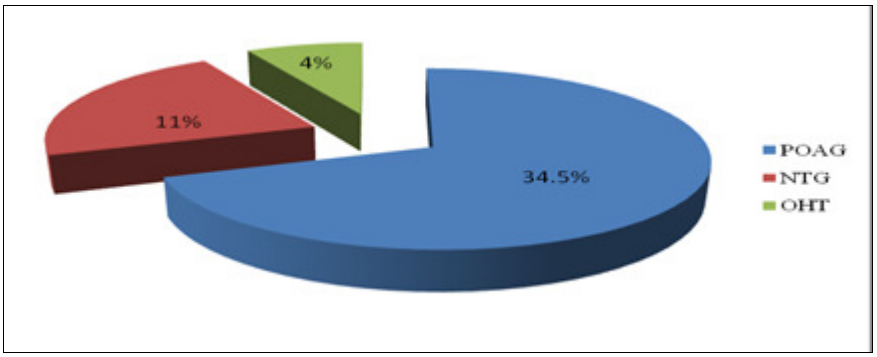

Figure 1: Classification of Glaucoma Eyes and Ocular Hypertensives According to IOP Measurement and Fundus Findings

Outcome Variable	Diagnosis				F Value	P Value
	POAG MEAN (SD)	NTG MEAN (SD)	OHT MEAN (SD)	NORMAL MEAN (SD)		
CCT	543.58 (37.4)	530.07 (33.1)	598.06 (6)	539.78 (24)	21.578	<0.001
IOP	27.65 (7.0)	14.52 (3.32)	25.06 (1.4)	16.33 (1.8)	206.41	<0.001
CORRECTED IOP	27.02 (6.4)	15.86 (3.4)	23.69 (1.3)	16.36 (2)	197.34	<0.001

Table 4: Comparison of CCT, IOP, Corrected IOP of Participants with Diagnosis

	Mean Difference	Standard Error	'P' Value
NORMAL VS OHT	-58.280	7.780	< 0.001
NORMAL VS POAG	-3.587	3.308	1.000
NORMAL VS NTG	9.350	4.984	0.368

Table 5: Post Hoc Analyses to Find Pair Wise Difference

Significant difference in the CCT was found between normal eyes and those with OHT. The CCT was marginally lower in those with NTG, while patients with POAG had no statistical difference in CCT compared to normal individuals.

5. Discussion

The present study is based on the determination of central corneal thickness (CCT) and its comparison between primary open angle glaucoma patients (POAG), normal tension glaucoma patients (NTG), ocular hypertensives (OHT) and normal subjects attending in the eye OPD.

Here we compared [pair wise] the mean CCT of POAG (543.37 with SD 37.39), NTG (530.43 with SD 33.43), OHT (598.06 with SD 5.93) and normal subjects (539.78 with SD 23.951).

There are already a few studies published on the effect of central corneal thickness on the measurement of intraocular pressure [11, 29, 30, 37]. All these studies reported higher central corneal thickness in ocular hypertensives than normal tension glaucoma, primary open angle glaucoma and normal subjects. Our study also replicated these findings. Even though Copt et al reported that CCT of NTG (521microns; SD=31) was significantly (p value <0.05) lower than POAG (543 microns; SD=35) and normal (552microns; SD=35) [],

we could not obtain a statistically significant result (p value >0.05). They also reported that there is no significant difference between POAG (543 microns; SD=35) and normal subjects (552microns; SD=35) which was similar to the present study [11].

A study done by Anupama C. Shetgar et al was similar to our study in which CCT of ocular hypertensives (OHT) (572.25 microns; SD=22.71) was higher than CCT of NTG (503.91 microns; SD=11.31), POAG (525.25microns; SD=23.59) and controls which was statistically significant (P value <0.05). Similar to the present study CCT of NTG was lower than the POAG and normal subjects and statistically not significant (p value = >0.05) [29].

Emara B. et al also revealed that central corneal thickness was significantly lower in normal tension glaucoma, CCT 513.2 (SD=26.1) than in chronic open angle glaucoma (COAG) CCT 548.2 (SD= 35.0) and the control group CCT of 556.7(SD=35.9) with significant p value ($p < 0.001$). No significant difference in corneal thickness was found between the chronic open angle glaucoma (COAG) and control groups which was similar to our study. Also the ocular hypertension (OHT) group had significantly thicker corneas 597.5(SD=23.6) than the three other groups which was statistically significant ($p<0.001$). Based on this they interpreted that patients with normal tension glaucoma may have thinner corneas than normal subjects and chronic open angle glaucoma. This may lead to the under estimation of their intraocular pressure. So corneal thickness should be taken into account while managing these patients to avoid under treatment [30].

In a study done by A.C. Ventura et al they included pseudo exfoliation glaucoma patients (13 subjects) in addition to normal tension glaucoma, primary open angle glaucoma, ocular hypertensives and normal. The CCT of normal tension glaucoma (518 microns; SD=0.5) and primary open angle glaucoma (515microns; SD=35) was almost similar in this study which was entirely different from other studies. The CCT of ocular hypertensives was 563microns ;(SD=29) and normal subjects (controls) was 524microns (SD=25). Similar to all the other studies CCT of ocular hypertensive patients was higher than the normal subjects, primary open angle glaucoma, normal tension glaucoma and pseudo exfoliation glaucoma [37].

The relationship between Goldmann applanation Tonometry and the central corneal thickness was investigated in several studies in the past and they have proved that the central corneal thickness affected the accuracy of the applanation tonometry.

Different formulas have been developed since then, to correct the IOP for the CCT**.** Ehlers and Hansen calculated the error which was evoked by a thinner or a thicker cornea to be 0.7mmHg per 10µ deviation from the normal value of 520µ [5]. Doughty's and Zaman's study showed that a 10% difference in the central corneal thickness (CCT) would result in a difference in the IOP ($p</= 0.001$, $r = 0.419$) of about 3.4 +/- 0.9 mm Hg [39].

A study by Shih C.Y. and Graff Zivin JS et al was based on an extensive literature review and 2.5 mmHg was added or subtracted for every 50 µ deviation in the CCT from the reference value [38]. In our study there is an inbuilt correction factor (Herdon's formula) for IOP incorporated in the pachymeter. The corrected IOP was measured and was used to identify patients who were previously wrongly labelled as NTG or OHT based on differences in corneal thickness.

6. Conclusion

The present study confirmed that ocular hypertension patients had significantly higher central corneal thicknesses than the primary open angle glaucoma, normal tension and normal patients.

The central corneal thickness of the normal tension glaucoma patients was lower as compared to that in the primary open angle glaucoma patients and normal subjects.

No significant difference in CCT was found between the primary open angle patients and the normal subjects.

Due to the effect of CCT on the measurement of IOP with Goldmann applanation tonometer many POAG patients may be misdiagnosed as NTG patients due to thin cornea and the normal subjects may be misdiagnosed as OHT patients due to thick cornea.

Measurement of the central corneal thickness helps the ophthalmologist in making a correct diagnosis and offers a better management of glaucoma and glaucoma suspects, especially when their corneal thicknesses differ markedly from the normal thickness.

The inclusion of CCT adjusted IOP during the management of glaucoma patients, will prevent over or under treatment of these cases.

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